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THE QUICK COMPONENT OF NYSTAGMUS

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THE swift return movement of the eye in ocular nystagmus, suggesting by its briskness the sudden release of a spring, is in striking contrast with the initial slow deviation. Because of this difference, and because a certain degree of narcosis will abolish the quick twitch without affecting the slow phase, the belief has arisen that the two components of nystagmus are subserved by quite different nervous mechanisms. It is now established that the impulses responsible for the slow deviation travel from the vestibular nuclei to the nuclei of the third, fourth and sixth cranial nerves via the posterior longitudinal bundle, the vestibulo-mesencephalic tract and possibly by other pathways in the substantia reticularis [de Nó, 1933; Löwenstein, 1937]. Until recently, there has been much difference of opinion as to the centres for the quick component, the suggested sites including the cerebral cortex [Bartels, 1910; Meyers, 1925], the thalamus [Wilson & Pike, 1912], the pons [Bárány, 1906], the primary vestibular nuclei [Spiegel, 1929], and the substantia reticularis [de Nó, 1933]. Most authorities now agree, however, that the rapid phase arises below the level of the oculomotor nucleus and outside the vestibular nuclei. But apart from the position of the "centre" for the quick component, there is another question of interest, namely, the origin of the rhythm of normal nystagmus. Is this motor rhythm a purely labyrinthine reflex, or is it controlled also by proprioceptive discharge from the eye muscles? Certainly each quick phase appears to be a compensatory movement, restoring the eyes approximately to the position from which the slow phase had displaced them. It is reasonable to consider the possibility that the quick component is a secondary reflex, set up when afferent endings in the orbit are stimulated by the mechanical changes comprising the slow component. This explanation was first given by Bartels [1911], and is at first sight attractive. The

extrinsic ocular muscles are known to be richly supplied with sensory endings [Tozer & Sherrington, 1910; Woollard, 1931]. It may well be imagined that stretch or contraction of these muscles during the slow deviation might set up afferent impulses capable of reflexly evoking a compensatory twitch, thus producing the rapid phase. Experimental proof of this hypothesis is difficult to obtain, because it has been shown that nearly all the afferent fibres supplying the ocular muscles run in the same nerve-trunks as the motor fibres, that is, in the third, fourth and sixth cranial nerves [Tozer & Sherrington, 1910; Woollard, 1931; Tarkhan, 1933]. Tozer & Sherrington state: "the fifth nerve may send a few fibres to the muscles in the orbit, but this supply in the rabbit, cat and monkey is insignificant in amount". Hence it is impossible to cut the afferent nerve fibres supplying the ocular muscles without severing the motor fibres as well. de Kleyn [1921] tried to overcome this difficulty by paralysing the proprioceptive endings with novocaine. In a decerebrate rabbit, he cut all the nerves to the ocular muscles except the sixth nerve on one side. The movements of the innervated lateral rectus were recorded on a kymograph. Caloric stimulation of one or other labyrinth produced contractions and relaxations of the muscle corresponding to the phases of nystagmus which would have occurred had the animal been intact. Finally, de Kleyn injected novocaine into the muscle, in the hope that the sensory endings would be paralysed before the motor. He argued that if the quick component depends on impulses from the periphery, there would be a period during which the muscle would show only the slow phase, the quick twitch having been abolished by paralysis of the afferent fibres from the muscle. In his experiments no such interval occurred, however; instead, after a short period of unchanged activity, all movement in the muscle ceased. Most authorities consider that this observation disproves Bartels' theory of the "muscular" origin of the rapid phase, but, though de Kleyn's findings are most suggestive, they can hardly be regarded as conclusive. It may well be doubted that an injection of novocaine into a muscle will paralyse every afferent fibre before affecting the motor fibres; certainly there is no way of proving whether this occurs. Thus de Kleyn's conclusions rest on a supposition, which may or may not be correct. Referring to this experiment, Maxwell [1923] writes: "...it does not appear to the writer to furnish positive proof of the central origin of both sets of impulses." Another doubt concerning the possible proprioceptive origin of the quick component has been expressed by Creed [1930]. The retractor bulbi muscle, found in most lower mammals, but not in primates, consists of four slips inserted

behind the recti muscles on the equator of the eyeball. Dusser de Barenne & de Kleyn [1928] have shown that these slips can produce nystagmus after all the other eye-muscles have been cut. The retractor bulbi is supplied mainly by the third nerve, though the sixth nerve sends some fibres to the lateral slip. Creed writes: "As a result of this discovery, it may perhaps be doubted how complete was the paralysis of all proprioceptive endings in contracting muscles when de Kleyn...applied novocaine to the isolated external rectus muscle." It is clear that further evidence is required before the question can be regarded as settled. To supply that evidence has been the aim of the present investigation.

Method

It is obvious that to be certain of eliminating the effect of all afferent endings in the extrinsic ocular muscles, the third, fourth and sixth nerves must be cut on both sides, a procedure which necessarily interrupts the entire motor pathway to these muscles. Hence there can be no mechanical changes available for recording during nystagmus. Fortunately, valve amplification gives us a method of recording the nervous activity responsible for nystagmus, even when the ocular muscles are disconnected from the brain stem. By placing electrodes on the central stump of one of the severed nerves, one can detect the motor impulses which would have produced the changes in muscle tension corresponding to the different phases of nystagmus had their whole pathway been intact. By this means, conclusive evidence may be obtained of the effect on nystagmus of the eye-muscle afferents. Cats were used throughout this investigation. Some preliminary experiments were made to determine the feasibility of recording action-potentials in the nerves to the ocular muscles. Filaments of the sixth nerve in the orbit were found to be the most suitable fibres for the purpose. The procedure of each experiment was as follows. Under ether anaesthesia, tracheotomy was performed, and the tracheal cannula connected to an automatic anaesthetic machine which maintained indefinitely the desired depth of ether narcosis. A transverse incision was then made across the vault of the skull, extending on each side to the lateral commissure of the eyelids. The temporal muscles were detached and turned down, after which an opening was made in the skull on each side, corresponding roughly to the area of attachment of the temporal muscle. After opening the dura, the frontal and temporal lobes were gently elevated until a clear view was obtained of the third and fourth nerves, which were then cut on each side. Cutting the oculomotor nerve produced, of course, pupillary dilatation and divergent

squint. Next, the bony and cartilaginous lateral walls of the orbits were removed. The recti and obliqui muscles were defined and cut, and the four slips of the retractor bulbi muscle were isolated and divided as far back in the orbit as possible. The optic nerves and ophthalmic arteries were ligated and cut and the eyeballs removed. Each sixth nerve was then isolated at its entrance into the orbit; one was left intact, with a loop of thread round it for identification, the other was followed to its termination in the lateral rectus. One of its terminal filaments was selected for recording and secured at its distal end with a fine silk ligature, then all connexions of the nerve with the muscle were severed. The head was clamped in a steel fixation frame in such a position that the lateral semicircular canals were approximately vertical, with the ampullae uppermost (i.e. with the head extended sixty degrees from its normal posture). In this position caloric stimulation of the labyrinth produces horizontal nystagmus. The grid lead from the amplifier was connected to the nerve filament under examination. The electrode consisted of a piece of silver-chloride coated silver wire, bent at the end into a hook which passed through a loop of Ringer-soaked thread surrounding the nerve filament. In some cats, the filament was long enough to be connected to both electrodes; in others, however, the available length of nerve would only permit the attachment of the grid electrode. The earthed lead in these cases was attached to the steel fixation apparatus, so making diffuse contact with the zygomatic arches and the vault of the skull. The amplifier consisted of four battery-operated triodes, resistance-capacity coupled, leading to a power pentode with a maximum output of 7·7 W. which was able to operate simultaneously a dynamic loudspeaker and a Matthews oscillograph. The power unit was operated from the 240 V. A.C. mains by means of a transformer, a rectifying valve and suitable smoothing devices. With the amplifier at one-half its maximum sensitivity, a rectangular input potential of 10μV. gave an oscillograph deflexion of 8 mm. falling to half its initial value in 0·05 sec. Most of the records were taken with the amplifier at one-half or one-quarter sensitivity. The preparation and the battery-operated stages of the amplifier were placed in a large earthed cage of fine wire-netting, to eliminate electrical interference. After listening to and recording the nerve-impulses associated with each phase of nystagmus produced by irrigation of one or other ear with hot or cold water, the intact sixth nerve was lifted up by its thread loop and cut, thus interrupting all the remaining motor fibres and almost all possible sensory pathways between the brain stem and the extrinsic ocular muscles. This procedure was carried out without disturbing the

electrodes or switching off the amplifier. The nerve discharges were again examined during labyrinthine stimulation to see if any change had occurred. Each animal was examined post-mortem to verify the completeness of the nerve section.

In a few instances, the mechanical changes in the innervated lateral rectus were recorded on the same sensitive paper as the action potentials in the opposite sixth nerve, by means of a light optical torsion myograph. In the upper record of Pl. I, Fig. 1 A, B, a contraction of the muscle produces an upstroke. In Fig. 1 A there is slow contraction followed by quick relaxation. In Fig. 1 B there is quick contraction and slower relaxation. The lower records of Fig. 1 A, B show the motor impulses in the nerve. Superimposed on the steady stream of impulses there are bursts of impulses in Fig. 1 A which are synchronous with the quick component of the nystagmus. In Fig. 1 B the muscle contracts during the quick component and the discharge of impulses in the opposite sixth nerve is synchronously diminished.

Results

No attempt was made to analyse in detail the nerve action potentials, but the following observations were made, relying as much on the auditory information provided by the loudspeaker as on the oscillograph records:

(1) With the animal under light ether narcosis, there was present a tonic discharge in all the nerves examined (record A, Pl. II, Fig. 2). The action potentials were of the order of 5–15 μV., and occurred at a frequency varying from 50 to 150 per sec. Since most of the nerve preparations contained a hundred or so fibres, this, of course, gives no indication of the impulse frequency in individual nerve fibres. The tonic discharge diminished or disappeared when the animal was deeply narcotized. This observation, and the disappearance of the impulses upon the death of the nerve, furnish strong evidence of their physiological origin. During the preliminary experiments, it was noticed that the tonic discharge in a sixth nerve connected to its muscle seemed to be no greater than the discharge present after severing the nerve distally. Thus it would appear that the tone of the extrinsic eye muscles, unlike that of other skeletal muscles, is very little influenced by proprioceptive impulses arising in the muscles themselves. On the other hand, labyrinthine stimulation invariably affected the tonic discharge even when narcosis was too deep for nystagmus to appear. Irrigation of the ipsilateral ear with cold water increased the frequency and intensity of the discharge; more and more groups of fibres began discharging until the noise in the loudspeaker

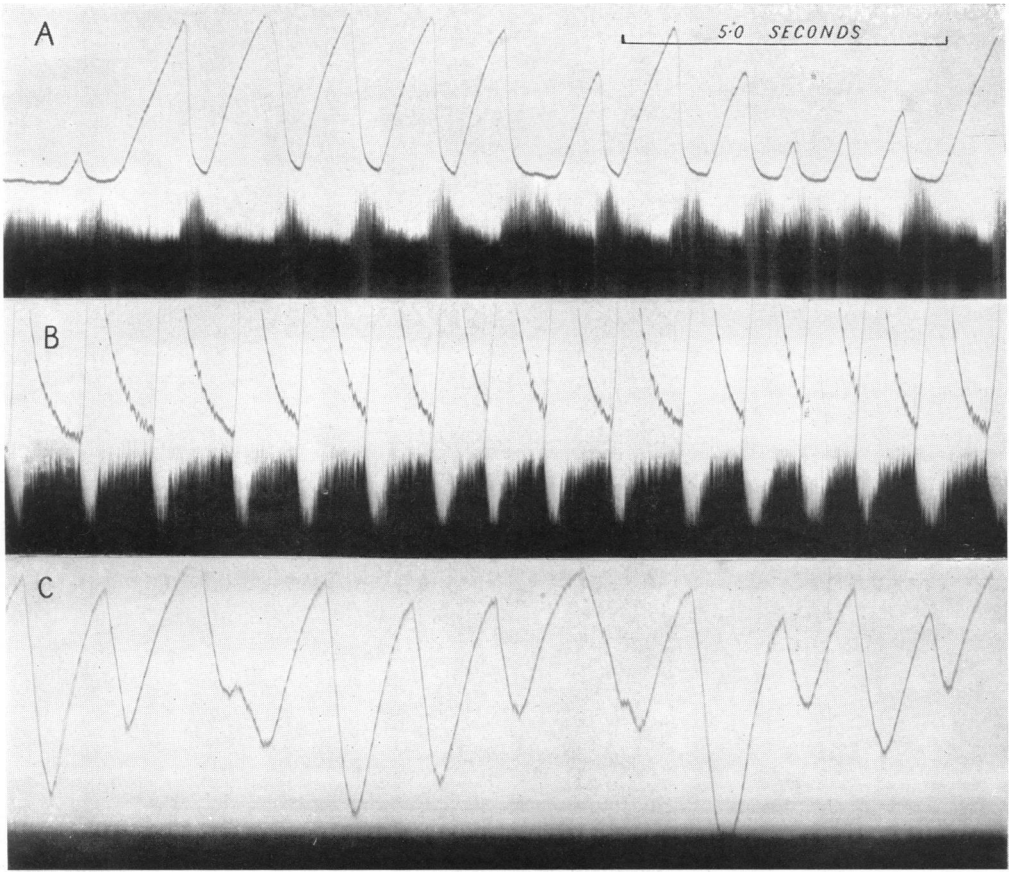

Fig. 1. Electrical activity in the left sixth nerve of a cat, photographed together with movements of the right lateral rectus muscle (the upper curve in each case). Contraction of the muscle produces an upstroke in the records, which read from left to right. A. Nystagmus with the quick component to the left. Each quick relaxation of the right lateral rectus is associated with a burst of impulse in the left sixth nerve. During each slow contraction of the muscle, the discharge of impulses gradually diminishes. B. Nystagmus with the quick component to the right. Each quick twitch of the right lateral rectus muscle is accompanied by a period of inhibition of the impulse-stream in the left sixth nerve. As the muscle relaxes, the discharge of impulses swells up to its full intensity. C. Control record of spontaneous nystagmus with the quick component to the left, taken after killing the left sixth nerve with ether. In spite of large excursions of the muscle, no associated electrical activity appears in the nerve. (Bromide paper moving at 2·3 cm./sec.)

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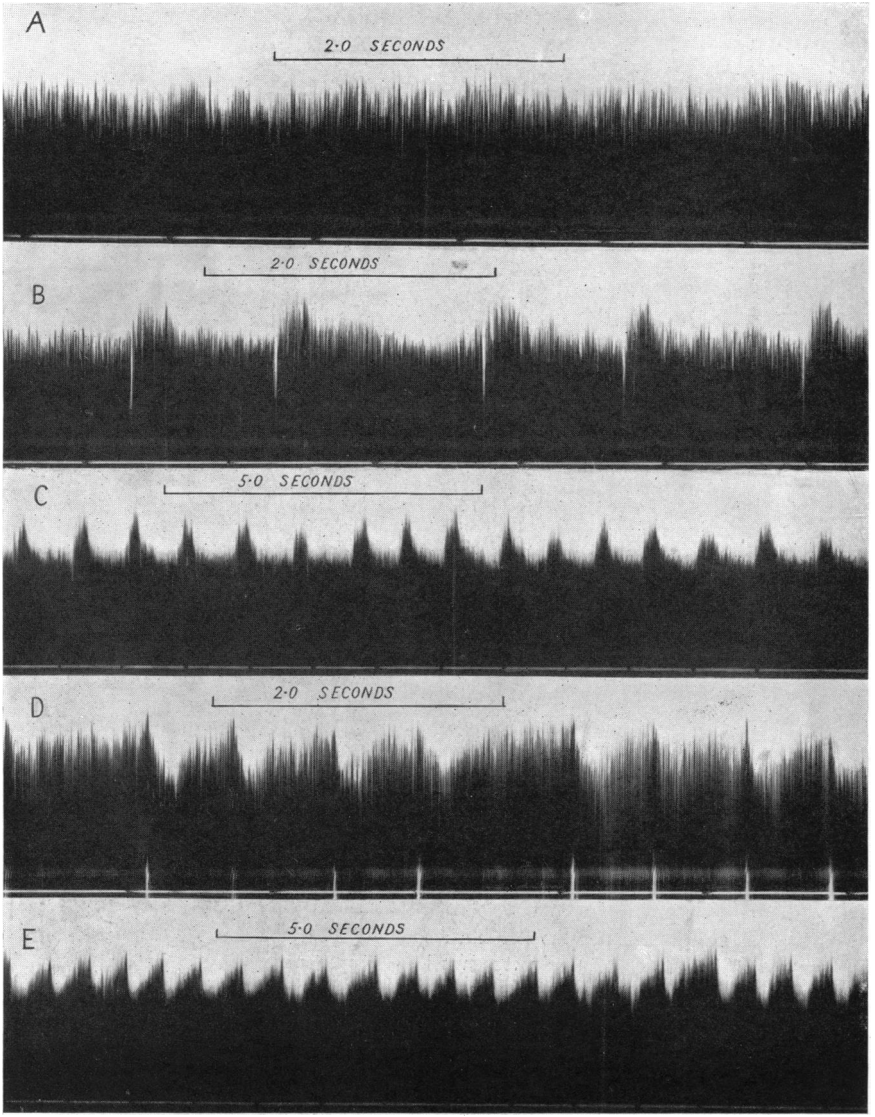

Fig. 2. Motor impulses in the right sixth nerve of a cat. A. Tonic discharge of impulses. B. "Nystagmus" to the right, showing quick component impulse-bursts (camera speed 5·2 cm./sec.). C. The same, photographed at a slower speed (2·3 cm./sec.). D. "Nystagmus" to the left, showing periods of diminished discharge corresponding to quick movements of the eyes to the left (camera speed 5·2 cm./sec.). E. The same, photographed with the bromide paper moving at 2·3 cm./sec. These patterns of electrical activity in the sixth nerve are characteristic of normal nystagmus, and undergo no change when all the nerves to the ocular muscles have been severed. All the records read from left to right.

became almost deafening and buzzing sounds indicated the presence of fibres discharging at high frequency. At this stage, irrigation of the same ear with hot water rapidly reduced the discharge to the discrete sounds of a few fibres firing at a slow rate. In some experiments, spontaneous nystagmus appeared when narcosis was very light, and often continued for several minutes. The nerve impulses associated with this spontaneous nystagmus were no different from those occurring during induced nystagmus.

(2) The impulses in the sixth nerve during nystagmus were quite characteristic. Irrigation of the right ear with hot water would normally produce a nystagmus with the slow phase to the left followed by a quick twitch to the right, that is to say, relaxation followed by rapid contraction in the right lateral rectus muscle. With the right sixth nerve connected to the amplifier, irrigation with hot water first produced a diminution in the frequency and amplitude of the tonic discharge corresponding to relaxation, followed by a loud burst of discharges corresponding to the quick twitch (Fig. 2B, C). The repetition of the cycle produced a series of bursts composed of synchronous volleys of impulses rather like those occurring in the phrenic nerve, except that each burst began abruptly and ended more gradually. At first there was only a slight tonic discharge between bursts, but as the effect of the irrigation passed off, the bursts themselves became smaller and less frequent, whilst the tonic discharge swelled up to its usual intensity.

Irrigation of the right ear with cold water would normally produce nystagmus with the quick twitch to the left, that is to say, slow contraction of the right lateral rectus followed by rapid relaxation. With the right sixth nerve connected to the amplifier, irrigation with cold water produced an increase in the amplitude and frequency of the tonic discharge representing the slow deviation of the eyes to the right. The augmented stream of impulses was then broken by a series of brief interruptions corresponding to the periods of relaxation of the muscle during the quick twitch to the left (Fig. 2D, E). This continued until the effect of the cold irrigation began to wane, whereupon the periods of inhibition became smaller and less frequent and were finally submerged in the tonic discharge. These changes in the action potentials corresponding to the quick and slow phases of nystagmus occurred as described only when the animal was lightly narcotized. With deeper anaesthesia, the bursts of impulses or periods of inhibition representing the quick component failed to appear, although there was no change in the augmentation or diminution of the tonic discharge during irrigation

corresponding to the slow phase. The slow component (tonic discharge) was abolished only by very deep narcosis.

(3) After cutting the intact sixth nerve, that is, the last sensorimotor pathway to the ocular muscles, the nystagmus action potentials were exactly the same as before. No detectable change occurred in the bursts of impulses or periods of inhibition representing the quick phases of nystagmus. In several instances, the intact sixth nerve was severed while nystagmic impulses in its fellow were being amplified, yet no alteration in the quick component impulse-bursts was ever detected during or after the procedure. Out of seven full experiments, five gave unmistakably the results just described. Labyrinthine stimulation could be repeated any number of times, always with the same effect. The other two experiments were not so clear-cut, because the results were not consistent. Although the usual variations in the tonic discharge occurred, the quick component impulse-bursts could be obtained only with the first few irrigations. However, the fact that there had been some quick component impulse-bursts after severance of all the nerves to the ocular muscles gives these two experiments some value, especially when taken in conjunction with the other results. It is possible that fatigue of or damage to the brain stem was responsible in these cases for the failure of normal "nystagmus" to appear after the first few irrigations.

Discussion

These observations place beyond doubt the truth of de Kleyn's assertion that the afferent endings in the ocular muscles play no essential part in normal nystagmus. In our experiments, all the efferent fibres and nearly all the afferent fibres were interrupted by cutting the third, fourth and sixth nerves on both sides. Even supposing that there were other significant sensory pathways from these muscles, they could have had no effect on the "nystagmus" in our preparations, because the necessary severance of all motor pathways prevented the occurrence of any muscle movements which might have stimulated proprioceptive endings. The retractor bulbi muscle slips were removed, and therefore need not be considered, even if some of their nerve-supply had escaped section when the third and sixth nerves were cut. It is quite clear, then, that the rhythmic phase alteration seen in normal nystagmus is entirely central in origin and could occur normally in the absence of any information from the eye muscle proprioceptors. Further, this information appears to be unnecessary for coordination of the different extrinsic eye muscles during

nystagmus. The behaviour of action potentials in the sixth nerve during nystagmus affords a striking illustration of the principle of reciprocal innervation. The gaps in the stream of impulses during nystagmus away from the side of the nerve under examination, and the fading of the tonic discharge with nystagmus of opposite direction show that reciprocal relaxation of the eye muscles does not depend on guidance from sensory endings therein.

It is interesting to note that the tonic discharge in the sixth nerve undergoes no apparent diminution when the nerve is severed distally. Thus it seems that the tonus of the eye muscles is not much influenced by the activity of their proprioceptive endings. Indeed, it would not be advantageous to the organism if the eye muscle tonus were constantly being altered by stretch reflexes, for the primary purpose of these muscles is not to keep constant the relation of the eye to the head, but to maintain as far as possible an unchanged visual field, until the cerebral cortex compels them to direct the eye elsewhere. Hence it is not surprising to find that the eye muscle tonus is determined chiefly by impulses from the ampullae of the semicircular canals and perhaps from other parts of the labyrinths [Löwenstein, 1936, 1937; Löwenstein & Sand, 1936], from the muscles, tendons and joints of the neck, and from the cerebral cortex. These impulses play on the third, fourth and sixth nerve nuclei in the brain stem.

Tozer & Sherrington have suggested that the function of the many delicate sensory endings in the extrinsic ocular muscles and tendons is to inform the cerebral cortex of the position of the eyes relative to the head. These authors have shown that one is still conscious of the position of the eyes in a dark room with the cornea and conjunctiva cocainized on both sides. The position in the brain stem of the cells responsible for the quick phase of nystagmus remains obscure, except that it lies below the level of the third nerve nuclei and outside the primary vestibular nuclei. Lorente de Nó regards nystagmus as being a rhythmic reflex analogous to the scratch reflex. When the labyrinth is stimulated, the primary vestibular nuclei discharge a continuous series of impulses which reach not only the eye muscle nuclei, causing the slow component, but also certain neurones in the reticular substance. These neurones can discharge only intermittently, being refractory until the vestibular impulses build up by recruitment the threshold excitatory state. With each discharge of impulses from these neurones, a quick reversal of the slow phase is produced. This conception of the mechanism of nystagmus seems to offer the best explanation of the known facts.

SUMMARY

1. Action potentials in the sixth cranial nerve have been studied, by means of an amplifier and Matthews oscillograph.

2. Under light ether narcosis, a tonic discharge of impulses was present in all the nerves examined. No change could be detected in the tonic discharge after cutting the nerve distally.

3. The motor impulses in the sixth nerve accompanying both phases of horizontal nystagmus were found to be characteristic.

4. After cutting the third, fourth and sixth nerves on both sides, and extirpating the retractor bulbi muscles, labyrinthine stimulation still produced in the central stump of the sixth nerve motor impulses characteristic of normal nystagmus.

5. These experiments, therefore, show beyond doubt the truth of de Kleyn's contention that the rhythm of normal nystagmus is entirely central in origin and is independent of impulses from the ocular muscles.

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